engineered constructs will alleviate the problems concerning the present treatment of cartilage diseases.

I-14
PROTEOMICS AS A TOOL FOR STUDYING OSTEOARTHRITIS

D. de Seny. *GIGA Res., Univ. of Liège, CHU Liège, Liège, Belgium*

Proteomics is the large-scale study of proteins expressed by cells, tissues or organ. It describes the dynamics of cell regulation by detecting molecular events related to the development of a disease. It is a multidisciplinary approach using medical, biological, bioanalytical and bioinformatics knowledge. One of the most promising applications of proteomics studies is identification of new biomarkers as indicators of pathogenic processes or pharmacologic responses to a therapeutic intervention. However, several practical considerations need to be raised to set up a robust and sensitive strategy for biomarker discovery in osteoarthritis (OA). OA is a heterogeneous, complex joint pathology. Progression of OA is slow and periodic with intermittent episodes of inflammatory flares and remission periods. Therefore, biomarkers are discontinuously released in biological fluids.
This presentation will focus on current proteomic approaches and their limitations in identifying the so-called soluble or "wet biomarkers" measured in blood, serum, plasma, urine and synovial fluid. The presence of a high quantity of proteins in such complex biological fluid make biomarkers discovery highly challenging. Nevertheless, current approaches exist to extend accessible concentration range and deep proteome detection. Comparison between a "targeted proteomic approach" based in the evaluation of single disease-related molecule levels and a "non-targeted proteomic approach" based on the simultaneous evaluation of hundreds proteins in a blind experiment using gel-based methods or mass spectrometry will be reviewed. Based on the assumption that a combination of biomarkers is more specific and sensitive for disease diagnosis than single marker, non-targeted proteomic technologies became highly attractive over the last decade. However, the gap between biomarkers discovery and clinical implementation remains important, as only few biomarkers have already been validated. All these practical considerations will be illustrated by current proteomics studies.

I-15
REHABILITATION FOR CARTILAGE DEFECT IN EARLY KNEE OA

M. Risberg. *NAR, Dept. of Sport Med., Norwegian Sch. Sport Sci., Oslo, Norway*

Background: It is well established that treatment and rehabilitation of patients with knee OA needs to start early in the disease process. Knee injuries and obesity have shown to be two of the most significant predictors for onset and progression of knee OA largely mediated by biomechanical forces acting across the knee. Articular cartilage in the knee is prone to damage by trauma or degeneration and damaged cartilage is one of the key issues in the OA disease process. Focal cartilage defects as well as other major knee injuries affect the mechanical environment in the joint possibly through changes in knee articular cartilage loading. The effect of exercise interventions for reducing symptoms and improving function in patients with knee OA has been well established, but the effect of exercise therapy for patients with focal cartilage defects is spares. Cartilage loading has shown to be significant for cartilage health, however, we lack knowledge on how muscle function affect cartilage health. Quadriceps muscle strength in particular has shown to influence load transmission and absorption across the knee joint
Objective: The objective of this presentation is to go through the evidence for the effect of exercises for patients with cartilage defect in early knee OA. Furthermore, the aim is to present the Oslo CARE study to highlight the need for specifically descried exercise therapy programs and how this exercise therapy program have shown to influence symptoms, disabilities and cartilage quality using quantitative MRI.
Methods: A narrative literature review will be presented as well as the development of the exercise therapy program and the outcomes from the Oslo CARE study. The Oslo CARE study included balance exercises, balance with resistance, followed by traditionally resistance training and finally plyometric exercises for patients with focal cartilage defects. The exercises aimed at generating muscle strength and power important for daily life and sport performance, without a potential deleterious effect on cartilage health.
Results: Clinically patients with focal cartilage defect experience pain, effusion, muscle weakness and other neuromuscular deficits. Furthermore, there is a wide range of the type, size and location of the patients' focal cartilage defect that should influence the type of exercises performed. It has been stated that conservative management of patients with cartilage defect are inappropriate since they are likely non-responders to such treatment. There are to our knowledge no RCTs on the effect of exercise therapy for patients with focal cartilage defects, but a few studies have examined the effect of exercises after cartilage repair. Different theories have been proposed for why exercises seem to work for patients with knee OA: neuromuscular, periarticular, intra-articular components, general fitness/health, and psychosocial. Studies seem to support that at least low to moderate activities and exercises improve function and are not deleterious to the knee articular cartilage. However, the mechanisms for why exercises seem to affect the patients' symptoms or function are not well understood. The Oslo CARE study showed that patients with focal cartilage defects improved knee function over time, without deleterious on the knee articular cartilage.
Discussion: We need to increase our focus on why exercises seem to work for patients with cartilage defects in early knee OA. We need to move from the palliative treatment of symptoms and dysfunction to a better understanding of how and if exercises affect the onset and progression of the knee OA process. Better rehabilitation programs for patients with focal cartilage defects, patients with significant predictors for development of knee OA, needs to be undertaken. The muscles of the lower extremity, particular the quadriceps, have shown to play an important role in the management of patients with knee OA.

I-16
ROLE OF COMPLEMENT AND INFLAMMATION IN OSTEOARTHRITIS

W. Robinson. *VA Palo Alto Hlth. Care System, Palo Alto, CA, USA*

Purpose: Although low-grade inflammatory responses are observed in OA, their contribution to its pathogenesis is unclear. We are investigating the role for the complement system and inflammation in the pathogenesis of OA.
Methods: Proteomic studies were performed on OA synovial fluids and membranes. Murine models of OA were used to further investigate the role of the complement system and other inflammatory mediators.
Results: Through proteomic analyses of synovial fluids and membranes from individuals with osteoarthritis, we find that expression and activation of complement and other inflammatory mediators in human osteoarthritic joints. Using mice genetically deficient in C5, C6, or CD59a, we show that complement, and specifically the membrane attack complex (MAC)-mediated arm of complement, is critical to the development of OA. Immunofluorescent staining demonstrated that MAC co-localized with matrix metalloprotease (MMP)-13 and with activated extracellular signal-regulated kinase (ERK) around chondrocytes in human osteoarthritic cartilage.
Conclusions: Our findings indicate that dysregulation of complement and activation of inflammatory pathways in synovial joints plays a critical role in the pathogenesis of osteoarthritis.

I-17
SYNDECAN-4: ENVIRONMENTAL SENSOR AND MATRIX REGULATOR

M.R. Morgan. *Univ. of Manchester, Manchester, United Kingdom*

Cell migration and microenvironment remodeling are essential for tissue morphogenesis, homeostasis and repair, and for the pathogenesis of inflammatory, neoplastic and degenerative musculoskeletal diseases. Adhesion contacts are integrin-mediated complexes that integrate the extracellular environment with the contractile machinery of the cell. Precise spatial and temporal coordination of adhesion complex dynamics is essential to permit efficient cell migration and to regulate extracellular matrix remodelling.
Differential engagement of $\alpha 5\beta 1$ and $\alpha V\beta 3$ integrins regulates the balance between adhesion contact turnover and stabilisation. However, the mechanisms that dynamically control heterodimer-specific delivery of integrins to the cell surface, in order to coordinate adhesion dynamics, are poorly understood. We have identified the membrane-intercalated proteoglycan syndecan-4, which serves a key role in the development of osteoarthritis, as the regulatory control point that coordinates integrin recycling.